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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/608,723	06/26/2003	Andrew R. Marks	0575/61134-B/JPW/AJM/AJD	6915

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EXAMINER	
LI, RUIXIANG	
ART UNIT	**PAPER NUMBER**
1646	

DATE MAILED: 04/27/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/608,723	MARKS, ANDREW R.	
	Examiner	Art Unit	
	Ruixiang Li	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 September 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) *7-12 and 19-24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6 and 13-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 June 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *01/30/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Invention group I, claims 1-6 and 13-18 in the reply filed on 09/16/2004 is acknowledged. The traversal is on the ground(s) that the inventions of Groups I-IV should be considered together because the claims of Groups I-IV all generally relate to treating or inhibiting the onset of, atrial tachyarrhythmia, using agents that affect various states. This is not found persuasive because groups I-IV are distinct inventions and claims of each invention group have different limitations. Invention group I requires administering an agent that inhibits PKA phosphorylation of a RyR2 receptor, whereas Invention group II requires administering an agent that mimics binding of a FKBP12.6 binding protein to a RyR2 receptor. Inventions III and IV are related Inventions I and II as product and process of use, respectively. Each invention group requires a separate search and consideration. Accordingly, examination of more than one group invention is an undue burden on the office.

   The requirement is still deemed proper and is therefore made FINAL.

2. Applicants' preliminary amendment filed on 06/26/2003 has been entered in full. Claims 25-54 have been canceled. Claims 1-24 are pending. Claims 1-6 and 13-18 are under consideration. All other claims are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being

no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 09/16/2004.

Information Disclosure Statement

3. The information disclosure statement filed on 01/30/2004 has been considered by the examiner and a signed copy has been attached to this office action

Drawings

4. The drawings filed on 06/26/2003 are accepted.

Claim Rejections—35 USC § 112, 1st paragraph

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-5 and 13-17 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for treating atrial tachyarrhythmia or inhibiting the onset of atrial tachyarrhythmia in a subject comprising administering to the subject a therapeutically effective amount of an agent that is disclosed in the specification or taught in the art (see below), does not reasonably provide enablement for such a method of employing a genus of agents that inhibits PKA phosphorylation of RyR2 receptor or dissociation of a FKBP12.6 from RyR2 receptor. The specification does not enable any person skilled in the art to which it pertains, or

with which it is most nearly connected, to make and use the invention commensurate in scope with the claims.

The factors that are considered when determining whether a disclosure satisfies enablement requirement include: (i) the quantity of experimentation necessary; (ii) the amount of direction or guidance presented; (iii) the existence of working examples; (iv) the nature of the invention; (v) the state of the prior art; (vi) the relative skill of those in the art; (vii) the predictability or unpredictability of the art; and (viii) the breadth of the claims. *Ex Parte Forman*, 230 USPQ 546 (Bd Pat. App. & Int. 1986); *In re Wands*, 858 F. 2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988).

Claims 1-5 are drawn to a method for treating a subject afflicted with atrial tachyarrhythmia comprising administering to the subject a therapeutically effective amount of an agent that inhibits PKA phosphorylation of RyR2 receptor or dissociation of a FKBP12.6 from RyR2 receptor, whereas claims 13-17 are drawn to a method for inhibiting the onset of atrial tachyarrhythmia in a subject comprising administering to the subject a prophylactically effective amount of an gent which inhibits PKA phosphorylation of RyR2 receptor or dissociation of a FKBP12.6 from RyR2 receptor. Thus, the claims are drawn to a method comprising administration of a genus of structurally undefined agents.

However, the specification merely discloses an agent, JTV-519, and other compounds derived from 1, 4-benzothiazepine (page 28, lines 31-34). The specification fails to provide the characteristic structure that is critical for the function of the claimed genus of agents and fails to provide sufficient guidance and/or working

examples on how to make such a genus of agents. The instant specification discloses that methods of screening for compounds to treat heart disease (page 45). However, a method of screening is not equivalent to a method of making an agent that that inhibits PKA phosphorylation of RyR2 receptor or dissociation of a FKBP12.6 from RyR2 receptor. While teaching a number of agents that inhibits PKA phosphorylation of RyR2 receptor or dissociation of a FKBP12.6 from RyR2 receptor (Reiken et al., *Circulation* 104:2843-2848, 2001; Doi et al., *Circulation* 105:1374-1379, 2002; Yano et al., *Circulation* 107:477-484, 2003), the prior art does not provide compensatory structural or correlative teachings to enable one skilled in the art to make the broad genus of agents. In view of the complexity of the nature of the work related to treating heart disease such as atrial tachyarrythmia, it is unpredictable, without a definitive structure, whether a compound has the property of inhibiting PKA phosphorylation of RyR2 receptor or dissociation of a FKBP12.6 from RyR2 receptor. Therefore, it would require undue experimentation for one skilled in the art to make the genus of agents and to use the agents in the claimed methods commensurate in scope with the claims.

7. Claims 1-5 and 13-17 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying

characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof.

Claims 1-5 are drawn to a method for treating a subject afflicted with atrial tachyarrhythmia comprising administering to the subject a therapeutically effective amount of an agent which inhibits PKA phosphorylation of RyR2 receptor or dissociation of a FKBP12.6 from RyR2 receptor, whereas claims 13-17 are drawn to a method for inhibiting the onset of atrial tachyarrhythmia in a subject comprising administering to the subject a prophylactically effective amount of an gent which inhibits PKA phosphorylation of RyR2 receptor or dissociation of a FKBP12.6 from RyR2 receptor. Thus, the claims are drawn to a method comprising administration of a genus of structurally undefined agents.

The specification fails to provide any critical structural feature to adequately describe the genus of agents that may be administered in the claimed methods. The specification merely discloses an agent, JTV-519, and other compounds derived from 1, 4-benzothiazepine (page 28, lines 31-34), which are not sufficiently representative of the claimed genus of agents. There is no defined relation between function and structure of the agents in the specification. There is even no identification of any particular portion of the structure that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the agents.

Furthermore, although teaching a number of agents that inhibits PKA phosphorylation of RyR2 receptor or dissociation of a FKBP12.6 from RyR2 receptor (Reiken et al., *Circulation* 104:2843-2848, 2001; Doi et al., *Circulation* 105:1374-1379, 2002; Yano et al., *Circulation* 107:477-484, 2003), the prior art does not provide compensatory structural or correlative teachings to enable one skilled in the art to identify the encompassed compounds as being identical to those instantly claimed.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of the agents used in the claimed methods, and therefore conception is not achieved until reduction to practice has occurred. Therefore, only the method of administering instantly disclosed and art-taught agents, but not the full breadth of the claims meets the written description provision of 35 U.S.C. §112, first paragraph.

Claim Rejections—35 USC § 112, 2nd Paragraph

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 2, 4-6, 14, and 16-18 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 2, 4-6, 14, and 16-18 are indefinite because they recite "a FKBP12.6 binding protein". While the specification defines the term "FKBP12.6", neither the specification nor the art defines "a FKBP12.6 binding protein" unambiguously, rendering the claims indefinite.

Claim Rejections—35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 1-6 and 13-18 are rejected under 35 U.S.C. 102(b) as being anticipated by Nakaya et al. (British Journal of Pharmacology, 131: 1363-1372, 2000), as evidenced by Yano et al. (*Circulation* 107:477-484, 2003).

Nakaya et al. teach inhibitory effects of JTV-519 on experimental atrial fibrillation in Langendorff-perfused guinea-pig hearts. Nakaya et al. teach that perfusion of carbachol (1 uM) shortened monophasic action potential and effective refractory period, and lowered atrial fibrillation threshhold of the guinea-pig hearts. Addition of JTV-519 (1 uM) inhibited the induction of atrial fibrillation by prolonging

monophasic action potential and effective refractory period (see, e.g., abstract). Nakaya et al. further that JTV-519 exerts antiarrhythmic effects against atrial fibrillation and may be useful for the treatment of patients with atrial fibrillation (see, e.g., abstract; bottom of page 1370). JTV-519 is known in the art to inhibit PKA phosphorylation of RyR2 receptor and dissociation of FKBP12.6 from the RyR2 receptor, as evidenced by Yano et al. (*Circulation* 107:477-484, 2003; in particular, pages 480-483). Thus, the reference of Nakaya et al. meets the limitations of claims 1-6 and 13-18.

Conclusion

12. No claims are allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ruixiang Li whose telephone number is (571) 272-0875. The examiner can normally be reached on Monday through Friday from 8:30 am to 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (571) 272-0829. The fax number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

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Ruixiang Li

Ruixiang Li, Ph.D.
Examiner
April 22, 2005